XV. *A Letter on the Differences in the Structure of Calculi, which arise from their being formed in different Parts of the urinary Passages; and on the Effects that are produced upon them, by the internal Use of solvent Medicines, from Mr.* William Brande *to* Everard Home, *Esq. F. R. S.*

Read, May 19, 1808.

DEAR SIR,

HAVING availed myself of the opportunity you procured for me, of making a chemical examination of the calculi contained in the HUNTERIAN MUSEUM, as well as those in your own collection, I herewith send you an account of what I have done.

Should the observations appear to you to throw any new light upon the formation of calculi, I request that you will do me the honour of laying them before the ROYAL SOCIETY.

The collection which I have examined, is not only uncommonly large, but the greater part of the specimens have histories of the case annexed to them.

This circumstance enabled me not only to ascertain the situations in which the calculi were found, but likewise many of the circumstances attendant on their formation.

I have therefore endeavoured to form an arrangement upon these principles, with a view to render the subject more clear and perspicuous.

## SECTION I.

*Of Calculi formed in the Kidnies, and voided without having afterwards undergone any Change in the urinary Passages.*

These have the following properties:

They are of a brownish yellow colour, sometimes of a grayish hue, which seems to arise from a small portion of dry mucus adhering to their surface.

They are entirely soluble in a solution of pure potash, and during their solution, they seldom emit an odour of ammonia.

When heated to dryness, with nitric acid, the residuum is of a fine and permanent red colour.

When exposed to the action of the blow-pipe, they blacken and emit a strong odour of burning animal matter, very different from that of pure uric acid. This arises from a variable proportion of animal matter which they contain, and which occasions the loss in the analysis of these calculi. Its relative quantity is liable to much variation, as may be seen from the following statements.

A calculus from the kidney, weighing seven grains, was dissolved in a solution of pure potash. A quantity of muriatic acid (rather more than sufficient for the saturation of the potash) was added, and the precipitate of uric acid thus obtained weighed when dry 4,5 grains. No other substance, except animal matter, which was evident on attempting to obtain the muriate of potash, could be detected, consequently the composition of this calculus was as follows:

| | Grs. |
|---|---|
| Uric acid - - | 4.5 |
| Animal matter - - | 2.5 |
| | 7.0 |

This is the largest proportion of animal matter which I have met with.

A small calculus from the kidney, weighing 3.7 grains, afforded by a like treatment 3.5 grains of uric acid, so that it was nearly a pure specimen of that substance.

The largest calculus of this kind which I have examined weighed seventeen grains; much larger ones have been found, but there is no evidence of their not having remained in the urinary passages for some considerable time. Thus Dr. HEBERDEN mentions one weighing twenty-eight grains.*

It often happens that the ingredients are not united together so as to form a calculus, but are voided in the state of a fine powder, commonly termed sand. This consists either of uric acid, or of the ammoniaco-magnesian phosphate, alone, or with the phosphate of lime.

I am induced to believe that the last mentioned substances, although the production of the kidnies, and held in solution, are never met with in a separate state till the urine has been at rest, and therefore, calculi from the kidnies are never composed of the phosphates.

In a few instances, calculi from the kidnies, composed of oxalate of lime, are voided; but this is a very rare occurrence: of three preserved in the HUNTERIAN Collection, two are

* Comment. on the Hist. and Cure of Diseases, 3d. edit. p. 88.

extremely small and hard, having an appearance of being made up of several smaller calculi, of a dark brown colour. The third is of the size of a small pea, its surface smooth, and of a gray colour, and not very hard.

## SECTION II.

### *Of Calculi which have been retained in the Kidney.*

When one or more of the calculi described in the preceding section are detained in the infundibula or pelvis of the kidney, it frequently happens that they increase in that situation to a considerable size.

This increase is of two kinds.

1. Where there is a great disposition to the formation of uric acid, the calculus consists wholly of that substance and animal matter, so as frequently to form a complete cast of the pelvis of the kidney.

2. Where there is less disposition to form uric acid, the external laminæ are composed of the ammoniaco-magnesian phosphate, and phosphate of lime.

In one instance, a small uric calculus had been deposited in the kidney, in such a situation that its upper surface was exposed to a continual stream of urine, upon which beautiful crystals of the triple phosphate had been deposited. It would therefore seem, that under common circumstances, a stream of urine passing over a calculus of uric acid, has a tendency to deposit the phosphate upon it.

## SECTION III.

### *Of Calculi of the urinary Bladder.*

Calculi met with in the bladder are of four kinds.

1. Those formed upon nuclei of uric acid, from the kidney.

2. Those formed upon nuclei of oxalate of lime, from the kidney.

3. Those formed upon sand or animal mucus, deposited in the bladder.

4. Those formed upon extraneous bodies introduced into the bladder.

They were arranged under the following divisions.

1. Calculi, which from their external appearance, consist chiefly of uric acid.

These calculi vary in colour from a deep reddish brown, to a pale yellowish brown.

They are either entirely soluble in a solution of pure potash, or nearly so.

During their solution they frequently emit the odour of ammonia.

When acetic acid is added to their alcaline solution, a precipitate possessing the properties of uric acid is obtained.

2. Calculi, composed chiefly of the ammoniaco-magnesian phosphate, or of phosphate of lime, or of mixtures of the two.

These calculi are externally of a whiter appearance than the former.

Some perfectly white, others gray, occasionally exhibiting small prismatic crystals upon their surface; others again soft and friable, a good deal resembling chalk. They are further characterised by their solubility in dilute muriatic acid.

3. Calculi, containing oxalate of lime; commonly called mulberry calculi.

These are distinguished by the difficulty with which they dissolve in dilute acids, by their hardness, and by leaving pure lime, when exposed to the action of the blowpipe.

In the examination of these calculi, I was struck with the small number of those strictly belonging to the first division, having been led, from the account of FOURCROY and VAUQUELIN,* and the experiments of Dr. PEARSON,† to believe that calculi, composed of pure uric acid, were by no mean unfrequent.

The greater number of the calculi examined by the former chemists, are stated to be completely soluble in the fixed alcaline leys; and of three hundred examined by Dr. PEARSON, a large proportion is said to consist of uric acid.

The following is a statement of the composition of the different calculi found in the bladder which I have examined.

16 were composed of uric acid.

45 ——————— uric acid with a small relative proportion of the phosphates.

66 ——————— the phosphates, with a relatively small proportion of uric acid.

12 ——————— of the phosphates entirely.

5 ——————— of uric acid, with the phosphates and nuclei of oxalate of lime.

6 ——————— chiefly of oxalate of lime.

150

* Annales de Chemie, xxxii. 218.

† Philos. Trans. 1798. p. 37.

To injure these calculi as little as possible, they were carefully cut through with a fine saw, and a portion of the whole cut surface removed by a file; in this way all the different ingredients of the calculi were obtained.

In the experiments upon uric calculi from the bladder, I found, in most instances, a far more considerable loss in attempting to obtain their pure uric acid, than in the kidney calculi, which led me to suppose that they contained urea and that the presence of this substance, with some of the salts of urine, and with small portions of the ammoniaco-magnesian phosphate, was the cause of the occasional evolution of ammonia when treated with the fixed alcalies, and of their easy solubility in those substances.

To determine this point a small calculus, weighing twenty-five grains, and of the species commonly supposed to consist of urate of ammonia,* was digested for two hours with water in a very moderate heat. The water which had assumed a pale yellow colour was filtered off, and fresh water added to the residuum three successive times, when it appeared that every thing soluble in that fluid was separated. The insoluble part of the calculus being now carefully dried and weighed, was found to have lost 5.5 grains.

The aqueous solution was evaporated by a gentle heat, nearly to dryness, and a substance was obtained having all the properties of urea, in combination with a small portion of muriate of ammonia, and of the ammoniaco-magnesian phosphate.

* Fourcroy observes that urate of ammonia is easily detected by its rapid solubility in the fixed alcalies, and the odour of ammonia, which is perceived during its solution.—Vide Thomson's Syst. of Chem. vol. v. p. 691.

Sixty grains of another calculus of a considerable size, supposed from a superficial analysis, to consist of nearly pure urate of ammonia, were digested at a low temperature in one ounce of alcohol. In an hour the alcohol was decanted off, and fresh portions were added successively, as long as it appeared to act upon the calculus, which after having been carefully dried in a temperature below 212°, weighed 54.8. grains, so that 5.2 grains had been taken up by the alcohol.

On evaporating the alcoholic solutions, a substance was obtained having all the properties of urea, with a small portion of saline matter, probably muriate of ammonia, as by the addition of potash, a slight ammoniacal odour was perceptible; its quantity however was too minute for accurate examination.

The remaining portion of the calculus, weighing 54.8 grains, was treated with small portions of acetic acid, by which 6. grains of the ammoniaco-magnesian phosphate were obtained.

The part of the calculus remaining after this treatment, weighing 48.8 grains was perfectly soluble in a solution of pure potash; it emitted no ammoniacal odour when acted upon by the alcali, and possessed the properties of pure uric acid.

The following therefore is the composition of this calculus.

| | Grains. |
|---|---|
| Urea, and muriate of ammonia - - | 5.2 |
| Ammoniaco-magnesian phosphate - | 6. |
| Uric acid - - - - | 48.8 |
| | 60. |

From these and many similar experiments upon other calculi, hitherto generally supposed to consist of urate of am-

monia, I am induced to believe that the evolution of ammonia depends in all instances upon the decomposition of the ammoniacal salts contained in the calculus, more especially of the ammoniaco-magnesian phosphate, and that no substance which can be called *urate of ammonia*, exists in calculi.

The mulberry calculus (oxalate of lime) I have but rarely met with. In those preserved in the HUNTERIAN Collection, there is a large relative proportion of phosphate of lime, and of uric acid. The purest of them afforded

| | Grains |
|---|---|
| Oxalate of lime - - | 65. |
| Uric acid - - | 16. |
| Phosphate of lime - - | 15. |
| Loss in animal matter . | 4. |
| | 100. |

When calculi of the urinary bladder increase to a very large size, they are generally composed of two or even three of the above mentioned varieties, the ammoniaco-magnesian phosphate being situated externally, and in the greatest abundance.

The largest calculus which I have seen, weighed, when recently removed from the bladder, twenty-three ounces and twenty-six grains. It consisted of a large mulberry or oxalate of lime calculus, the nucleus of which was uric acid, surrounded by a considerable quantity of the ammoniaco-magnesian phosphate in a very pure state.

Another very large calculus, weighing fifteen ounces and a half, consisted of a nucleus of uric acid, enveloped in the ammoniaco-magnesian phosphate, not however pure, but intersected by several laminæ of uric acid.

Four distinct substances are extremely rare in calculi; I have seen one in which the uric acid, the ammoniaco-magnesian phosphate, the phosphate of lime, and the oxalate of lime, were all in perfectly separate and distinct layers.

Four calculi, having the following extraneous substances for their nuclei were examined.

1. A common garden pea.
2. A needle.
3. A hazle nut.
4. A part of a common bougie.

In the two first instances, the calculous depositions were of a pale gray colour, inclining to white; soft and friable in their texture, and entirely soluble in muriatic acid.

The composition of the first was as follows;

| | Grains. |
|---|---|
| Phosphate of lime - - | 65. |
| Ammoniaco-magnesian phosphate - | 28. |
| Loss - - - - | 7. |
| | 100. |

Of the second;

| | |
|---|---|
| Phosphate of lime - - | 45. |
| Ammoniaco-magnesian phosphate - | 38. |
| Oxalate of lime - - - | 12. |
| Loss - - - - | 5. |
| | 100.* |

The deposition of calculous matter upon the bougie was covered with blood, and in very small quantity, the bougie

* It appears that in this case there had been an accidental disposition to the formation of oxalate of lime.

having been removed by an operation soon after it had passed into the bladder. It appeared to consist chiefly of phosphate of lime.

The incrustation upon the hazel nut was also destitute of uric acid.

## SECTION IV.

### *Of Calculi of the Urethra.*

All those that were examined had escaped from the bladder while very small, and had afterwards lodged in the membranous part of the urethra, where they had increased in size, and formed a cavity in which they were more or less embedded.

Two of these calculi were broken.

The fragments consisted in one instance, of ammoniaco-magnesian phosphate, and phosphate of lime, with a small portion of uric acid: and in the other the fragments were composed entirely of the ammoniaco-magnesian phosphate.

The third calculus was of a very remarkable appearance; its form being that of a perfect sphere, about half an inch in diameter. It was coated with small but very regular crystals of the triple phosphate in its purest state. On account of the singularity of the form and external appearance of this calculus, it was not sawn through; the nucleus, in all probability, is a small kidney calculus, which lodging in the urethra has become coated with triple phosphate.

## SECTION V.

### *Analysis of Calculi from other Animals.*

1. The Horse.

A. *From the kidney.*

A very large calculus, from the kidney of a horse, was composed of

| | |
|---|---|
| Phosphate of lime - - | 76 |
| Carbonate of lime - - | 22 |
| | 98. |

B. *From the bladder.*

This calculus was also of a large size, its weight when perfectly dry, nine ounces and a half, its external surface very irregular, of a reddish brown colour, and covered with minute crystals of the ammoniaco-magnesian phosphate. On making a section of it, the internal structure exhibited a radiated appearance, and was of a light brown colour. It consisted of

| | |
|---|---|
| Phosphate of lime - - | 45. |
| Ammoniaco-magnesian phosphate - | 28. |
| Animal matter - - - | 15. |
| Carbonate of lime - - - | 10. |
| | 98. |

In another case the bladder of a horse was found to be nearly full of sand, the composition of which was as follows:

| | |
|---|---|
| Phosphate of lime - - | 60. |
| Carbonate of lime - - | 40. |
| | 100. |

2. THE OX.

A number of small calculi from the size of a pea downwards, are not unfrequently found in the bladder of the ox. Those in the HUNTERIAN Collection are of a pale brown colour, and of the size just mentioned; some of them have the mulberry appearance.

They consist of carbonate of lime and animal matter, which last substance retains the form of the calculus, after it has been acted upon by diluted acids.

3. The Sheep.

A calculus from the kidney of a sheep was composed of

| | |
|---|---|
| Phosphate of lime - - | 72. |
| Carbonate of lime - - | 20. |
| Animal matter - - | 8. |
| | 100. |

4. The Rhinoceros.

The urine of this animal is exceedingly turbid at the time it is voided, and when allowed to remain at rest, deposites a very large proportion of sediment, which consists of carbonate of lime, with small portions of phosphate of lime and animal matter.

5. The Dog.

A large calculus from the bladder of a dog twenty years old, weighing sixteen ounces, was extremely hard, and of a gray colour; when cut through, it exhibited a nucleus about the size of a hazel nut, partly made up of concentric layers of phosphate of lime, and partly of crystals of the ammoniaco-magnesian phosphate. The part of the stone surrounding the nucleus consisted of

| | |
|---|---|
| Phosphate of lime - - - | 64. |
| Ammoniaco-magnesian phosphate - | 30. |
| Animal matter - - - | 6. |
| | 100. |

Sand taken from a dog's bladder was of a gray colour, and contained

| | |
|---|---|
| Carbonate of lime - - | 20. |
| Phosphate of lime - | 80. |
| | 100. |

6. THE HOG.

A calculus from the bladder of this animal weighed nineteen drachms; it was of a pale gray colour inclining to white, and so hard that it was with difficulty cut through. Its internal structure was uniform, and there was no appearance of a nucleus. It was composed of

| | |
|---|---|
| Carbonate of lime - | 90. |
| Animal matter - - | 10. |
| | 100. |

7. THE RABBIT.

A calculus from the rabbit's bladder weighing four drachms, was of a dark gray colour, and appeared as if composed of several smaller calculi. It consisted of

| | |
|---|---|
| Phosphate of lime - | 39. |
| Carbonate of lime - - | 42. |
| Animal matter - | 19. |
| | 100. |

## SECTION VI.

### *General Inferences.*

It appears from the preceding observations, that calculi formed in the kidnies, and immediately voided, are almost always composed of uric acid; and that the phosphates are very frequent ingredients in calculi of the bladder, more especially in those, which, from their situation, have been exposed to a continual current of urine: they also uniformly are

deposited upon extraneous substances introduced into the bladder, but appear never to form small kidney calculi.

In what is commonly called a fit of the gravel, a small uric calculus is formed in the kidney, and passes along the ureter into the bladder.

It is found from observation, that for some time after a stone has passed from the kidney, the urine is generally unusually loaded with uric acid, and deposites that substance upon the nucleus now in the bladder. When this period, which is longer or shorter in different individuals, has elapsed, the subsequent addition to the calculus consists principally of the phosphates.

Where the disposition therefore to form uric acid in the kidnies is very great and permanent, the calculus found in the bladder is principally composed of uric acid; but where this disposition is weak and of short duration, the nucleus only is uric acid, and the bulk of the stone is composed of the phosphates.

Where the increased secretion of uric acid returns at intervals, the calculus is composed of alternate layers of uric acid and the phosphates.

Other small calculi being formed in the kidney, make their way into the bladder, and afford fresh nuclei; so that several calculi are sometimes found in the same bladder, and their composition is usually nearly the same.

In other cases it happens, that a constant increased secretion of uric acid is going on from the kidnies, only in small quantity, which will be more uniformly mixed with the phosphates deposited in the bladder, and where the uric acid predominates, the species of calculus denominated improperly, *urate of ammonia*, will be produced.

We are entirely ignorant of the cause of the formation of the oxalate of lime, or mulberry calculus. I have frequently looked for oxalate of lime in the urine of calculous patients, but have never been able to detect it, and as it does not exist in healthy urine, it must be regarded as a morbid secretion. Its mode of formation seems to resemble that of uric acid, since small kidney calculi, composed of oxalate of lime, have in a few instances been voided; and in these cases, as far as my own enquiries go, the persons have been much less liable to a return of the complaint, than where uric calculi have been voided.

In some rare instances we meet with calculi of the bladder which are destitute of uric acid, and of oxalate of lime, the nucleus being composed of a little loosely agglutinated ammoniaco-magnesian phosphate, and the whole calculus consisting of that substance, with variable portions of phosphate of lime: in two cases I have met with calculi of this kind, composed of the triple phosphate only: they seem to be entirely formed in the bladder.

Having taken this short view of the formation of calculi, I shall now enquire into the action of solvents, employed either with a view of effecting their solution, or of preventing their formation and increase.

Solvents are of two kinds.

1. Alkaline. 2. Acid.

In the exhibition of these, the practitioner is usually guided by the chemical composition of the calculous matter voided by urine.

The different kinds of gravel voided by persons labouring under calculous complaints, may be classed in two divisions.

1. *Uric acid,* either in a pure state, or with a very small proportion of the phosphates.

2. *The phosphates,* either pure, or with a small proportion of uric acid.

The first species, which generally appears in the form of minute crystalline grains, of a reddish brown colour, or of an impalpable brown powder, is either entirely soluble in pure alkaline solutions, not emitting an ammoniacal odour, in which case it consists of pure uric acid: or it does emit an ammoniacal odour, and is not entirely soluble, in which case it contains the triple phosphate of ammonia and magnesia.

When this substance is observed in the urine, the alkalies are recommended. They are exhibited either in a pure state, or as carbonates, and in each instance the uric sediment generally diminishes rapidly, and during the continued use of alkaline medicines, occasionally disappears altogether.

It however frequently happens that the matter voided, is not diminished in quantity by the use of alkalies, but that its form and composition are altered, and that it assumes the appearance of a gray powder, and is composed of uric acid with variable portions of the ammoniaco-magnesian phosphate.

From these facts therefore, it cannot be doubted that the internal exhibition of alkalies, often prevents the formation of uric acid, and hence must likewise prevent the increase of a calculus in the bladder, as far at least as uric acid is concerned; but it has also been supposed that the alkalies are capable of acting upon the stone itself, and even of effecting its complete solution. It is true that if we immerse a calculus, composed of uric acid, in a dilute solution of caustic alkali, that it will be slowly acted upon, and after some time entirely dissolved.

If however we attend to what would take place in the body, we shall find the circumstances very different.

That alkaline carbonates and sub-carbonates exert no action upon uric acid I consider to be completely established, both by the experiments of several eminent chemists, and those I have myself made upon the subject; and as there is at all times a quantity of uncombined acid in the urine, it follows that although the alcali may arrive at the kidnies in its pure state, it will there unite with the uncombined acid, and be rendered incapable of exerting any action upon the calculus in the bladder. Besides phosphoric acid, the urine always contains a quantity of uncombined carbonic acid; this is proved by placing a quantity of recently voided urine under the receiver of an air pump; during the exhaustion, a large quantity of carbonic acid gas makes its escape: and when urine is distilled at very low temperatures, carbonic acid gas is given off: and also, when lime water is poured into urine, a precipitate appears, consisting of phosphate and carbonate of lime.

Lime water, on account of the insoluble compounds which lime forms with carbonic, and phosphoric acids, is even more objectionable as a solvent, than the alkalies.

It may however be said, that if these means prevent the increase of a calculus, material relief is afforded to the patient. How far the exhibition of alkaline remedies can be recommended upon these grounds, will appear, when the circumstances which attend the formation of the second species of calculous sediment or deposition in the urine, are considered.

The ammoniaco-magnesian phosphate appears under two forms: it is either voided in a solid state, or in solution. In the former case it bears a good deal of resemblance to a white

sand, and is frequently mixed with variable proportions of phosphate of lime. In the latter it makes its appearance after the urine has remained undisturbed for some hours in an open vessel, generally in the form of a fine pellicle, or of crystalline laminæ, which when collected and dried bear some resemblance to boracic acid.

Its putting on this form is accounted for, from its being held in solution in the first instance by carbonic acid, and as this flies off, the triple salt makes its appearance. If a portion of the urine be preserved in a phial closely stopped, the carbonic acid cannot escape, and consequently no phosphate is observed to separate. There is also a quantity of phosphoric acid present, which keeps another portion of the ammoniaco-magnesian phosphate, and also some lime (in the state of super phosphate of lime) in solution.

It is therefore obvious, that whenever the urine is deprived of a portion of the acid which is natural to it, the deposition of the triple phosphate, and phosphate of lime, more readily takes place: this is effected by the exhibition of the alkalies.

It may therefore be asserted, that although alkaline medicines often tend to diminish the quantity of uric acid, and thus to prevent the addition of that substance in its pure state, to a calculus in the bladder; they favour the deposition of the phosphates.

It cannot be doubted that the alkalies reach the bladder, since in cases where large doses of sub-carbonate of potash have been exhibited, I have seen evident traces of it in the urine.

Where the phosphates only are voided, it has been pro-

posed to dissolve the calculus by the exhibition of acids, and more especially the muriatic acid.

During the use of the muriatic acid, the phosphates are either diminished or disappear altogether; and even sometimes the urine acquires an additional acidity: a solution of that part of the calculus which consists of the phosphates might therefore be expected; but even then the nucleus of uric acid would remain, and thus a great deal of time would be lost without any permanent advantage.

I have also occasionally remarked, that during the use of acids, the uric acid re-appears, and even seems to be augmented in quantity.

Attempts have been made at different times to effect the solution of calculi, by the injection of solvents into the bladder. This subject has been more lately revived by FOURCROY and VAUQUELIN, who, in their paper on the composition of calculi, lay down rules for its practice. Independent, however, of the impossibility of ascertaining the composition of the calculus with sufficient accuracy, it is obvious, that were the composition of the surface of the calculus known, the frequent introduction of an instrument into the bladder, and the long continuance of the process which would be necessary, even where the calculi are small, are insurmountable objections; and whenever this mode of treatment has been adopted, it has speedily been relinquished, as it always aggravates the sufferings of the patient.

It has been shewn that in the majority of cases, the nuclei of calculi originate in the kidnies, and that of these nuclei by far the greater number consist of uric acid; the good effects

therefore so frequently observed during the use of an alkali, arise, not from any actual solution of calculous matter, but from the power which it possesses of diminishing the secretion of uric acid, and thus preventing the enlargement of the calculus, so that, while of a very small form, it may be voided by the urethra.